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Fig. 9 is a restriction map of the plasmid pAF100. (See also YEAST, 6:521-534, 1990, which is relied upon and incorporated by reference herein). Figs. 10A and 10B show the nucleotide sequence and restriction sites of regions of the plasmid pAF100 (SEQ ID NOS: 45-50). --

On page 12, replace the last paragraph with the following new paragraph:

-- The enzyme I-Scel has a known recognition site. (ref. 14.) The recognition site of I-Scel is a non-symmetrical sequence that extends over 18 bp as determined by systematic mutational analysis. The sequence reads: (arrows indicate cuts)

5' TAGGGATAACAGGGTAAT 3' (SEQ ID NO:51)

3' ATCCCTATTGTCCCATTA 5' (SEQ ID NO:52). -

On pages 41 to 42, replace the bridging paragraph with the following:

-- -e- The supernatant of this clone was used to infect other mouse cells (1009) by spreading 10⁵ virus particles on 10⁵ cells in DMEM medium with 10% fetal calf serum and 5 mg/ml of "polybrene" (hexadimethrine bromide). Medium was replaced 6 hours after infection by the same fresh medium. --

After page 52, and before page 53, please insert the attached pages titled SEQUENCE LISTING".

<u>IN THE CLAIMS</u>

Please cancel claims 1-26.

Please add the following new claims:

- --27. A method for *in vivo* site directed genetic recombination in an organism comprising:
- (a) providing a transgenic cell having at least one HO endonuclease or Group I intron encoded endonuclease recognition site inserted at a unique location in a chremosome;

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transgenic cell;

(b) providing an expression vector that expresses said endonuclease in said

- (c) providing a plasmid comprising a gene of interest and a DNA sequence homologous to the sequence of the chromosomal DNA, allowing homologous recombination;
 - (d) transfecting said transgenic cell with said plasmid of step (c);
 - (e) expressing said endonuclease from said expression vector in said cell; and
- (f) cleaving said endonuclease recognition site with said endonuclease, whereby said cleavage promotes the insertion of said gene of interest into said chromosome of said organism at a specific site by homologous recombination.
- 28. The method of claim 27, wherein said endonuclease recognition site has been introduced into said cells by homologous recombination.
- 29. The method of claim 27, wherein said endonuclease recognition site has been introduced into said cells by retroviral insertion.
 - 30. The method of claim 27, wherein said organism is yeast.
 - 31. The method of claim 27, wherein said organism is bacteria.
 - 32. / The method of claim 27, wherein said organism is a mammal.
- 33. The method of claim 27, wherein said endonuclease site is a Group I intron encoded endonuclease site.



